10/806,327

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	917	$4amphetamine same (determin$5 or detect$3)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/05/23 15:19
L2	401	l1 and antibody	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/05/23 15:19
L3	273	l2 and link$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/05/23 15:21
L4	16	l3 and bivalent	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2005/05/23 15:22

10/806,327

FILE 'HOME' ENTERED AT 14:23:23 ON 23 MAY 2005

=> FIL REGISTRY
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:23:31 ON 23 MAY 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 MAY 2005 HIGHEST RN 850859-04-0
DICTIONARY FILE UPDATES: 22 MAY 2005 HIGHEST RN 850859-04-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

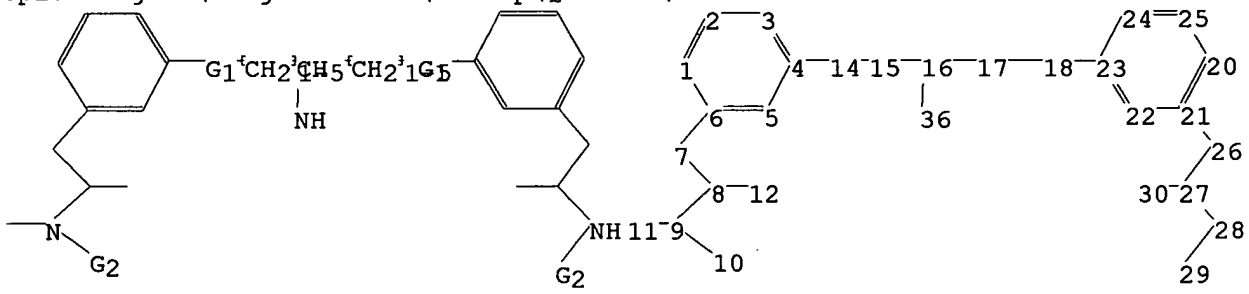
Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10806327.str



chain nodes :
7 8 9 10 11 12 14 15 16 17 18 26 27 28 29 30 36
ring nodes :
1 2 3 4 5 6 20 21 22 23 24 25
chain bonds :
4-14 6-7 7-8 8-9 8-12 9-10 9-11 14-15 15-16 16-17 16-36 17-18 18-23
21-26 26-27 27-28 27-30 28-29

ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 20-21 20-25 21-22 22-23 23-24 24-25
exact/norm bonds :
4-14 8-9 9-10 9-11 14-15 16-36 17-18 18-23 27-28 28-29
exact bonds :
6-7 7-8 8-12 15-16 16-17 21-26 26-27 27-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 20-21 20-25 21-22 22-23 23-24 24-25
isolated ring systems :
containing 1 : 20 :

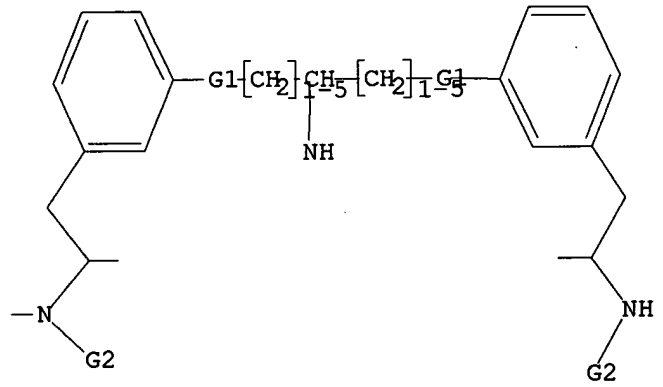
G1:O,S

G2:Ak,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 36:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,S
G2 Ak,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:24:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 289 TO ITERATE

100.0% PROCESSED 289 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4761 TO 6799
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

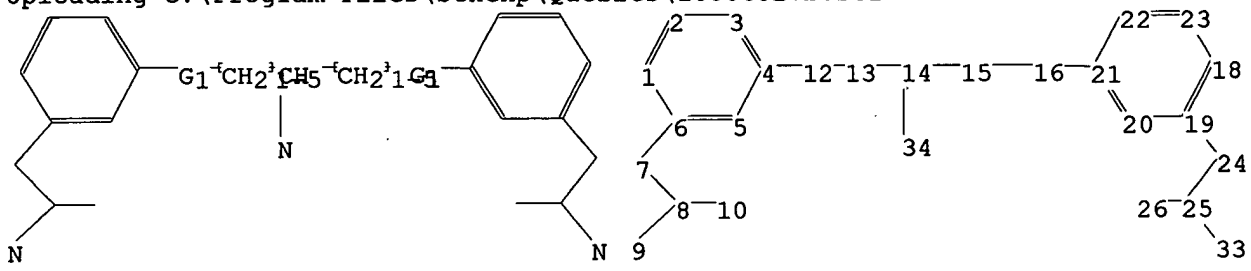
=> s li sss full
99643 LI
16507 LIS
L3 116146 LI
(LI OR LIS)

=> s l1 sss full
FULL SEARCH INITIATED 14:25:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5455 TO ITERATE

100.0% PROCESSED 5455 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.02

L4 0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10806327b.str



chain nodes :
7 8 9 10 12 13 14 15 16 24 25 26 33 34
ring nodes :
1 2 3 4 5 6 18 19 20 21 22 23
chain bonds :
4-12 6-7 7-8 8-9 8-10 12-13 13-14 14-15 14-34 15-16 16-21 19-24 24-25
25-26 25-33
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 18-19 18-23 19-20 20-21 21-22 22-23
exact/norm bonds :
4-12 8-9 12-13 14-34 15-16 16-21 25-33
exact bonds :
6-7 7-8 8-10 13-14 14-15 19-24 24-25 25-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 18-19 18-23 19-20 20-21 21-22 22-23
isolated ring systems :
containing 1 : 18 :

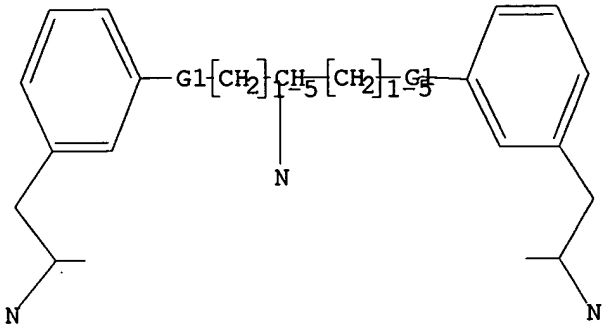
G1:O,S

G2:Ak,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS 33:CLASS 34:CLASS

L5 STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5 STR



G1 O,S

G2 Ak,H

Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 14:28:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 251 TO ITERATE

100.0% PROCESSED 251 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4070 TO 5970
PROJECTED ANSWERS: 0 TO 0

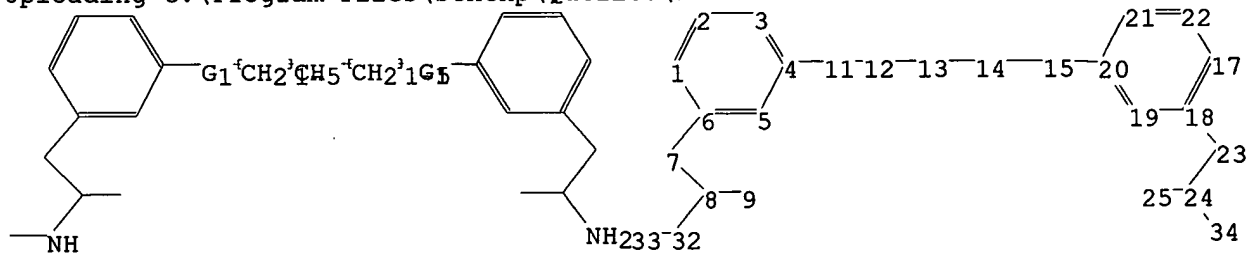
L6 0 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 14:29:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 4599 TO ITERATE

100.0% PROCESSED 4599 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L7 0 SEA SSS FUL L5

=>
Uploading C:\Program Files\Stnexp\Queries\10806327c.str



chain nodes :
7 8 9 11 12 13 14 15 23 24 25 32 33 34
ring nodes :
1 2 3 4 5 6 17 18 19 20 21 22
chain bonds :
4-11 6-7 7-8 8-9 8-32 11-12 12-13 13-14 14-15 15-20 18-23 23-24 24-25
24-34 32-33
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22
exact/norm bonds :
4-11 8-32 11-12 14-15 15-20 24-34 32-33
exact bonds :
6-7 7-8 8-9 12-13 13-14 18-23 23-24 24-25
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22
isolated ring systems :
containing 1 : 17 :

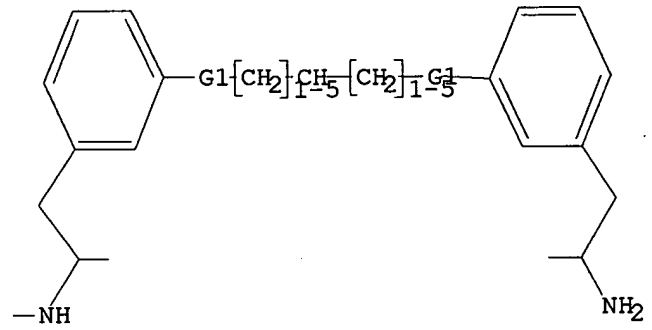
G1:O,S

G2:Ak,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:CLASS 24:CLASS 25:CLASS 32:CLASS 33:CLASS 34:CLASS

L8 STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8 STR



G1 O,S
G2 Ak,H

Structure attributes must be viewed using STN Express query preparation.

=> s l8
SAMPLE SEARCH INITIATED 14:33:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 291 TO ITERATE

100.0% PROCESSED 291 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4797 TO 6843
PROJECTED ANSWERS: 0 TO 0

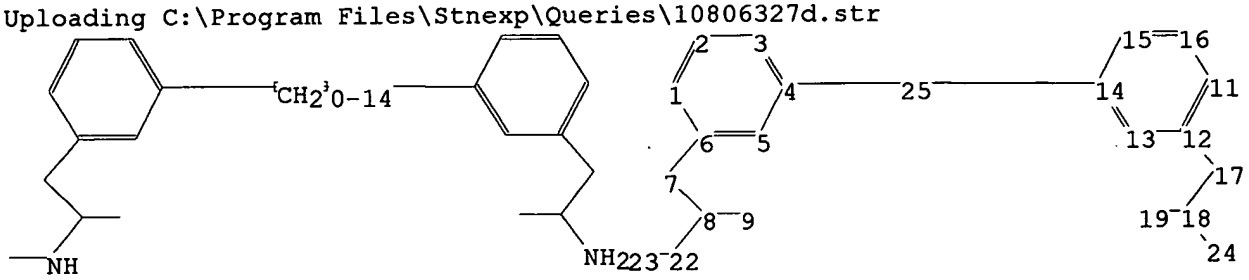
L9 0 SEA SSS SAM L8

=> s l8 sss full
FULL SEARCH INITIATED 14:33:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5472 TO ITERATE

100.0% PROCESSED 5472 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L10 0 SEA SSS FUL L8

=>
Uploading C:\Program Files\Stnexp\Queries\10806327d.str



chain nodes :
7 8 9 17 18 19 22 23 24 25
ring nodes :
1 2 3 4 5 6 11 12 13 14 15 16
chain bonds :
4-25 6-7 7-8 8-9 8-22 12-17 14-25 17-18 18-19 18-24 22-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16
exact/norm bonds :
8-22 18-24 22-23
exact bonds :
4-25 6-7 7-8 8-9 12-17 14-25 17-18 18-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

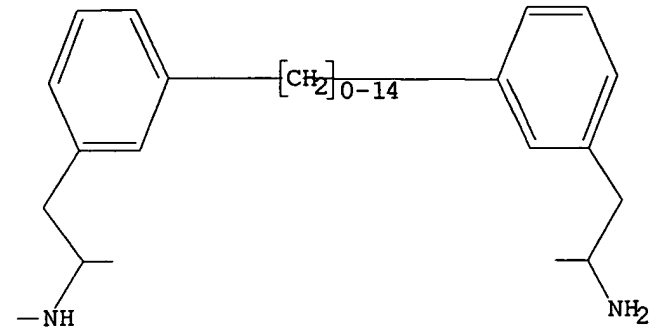
G1:O,S

G2:Ak,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 22:CLASS
23:CLASS 24:CLASS 25:CLASS

L11 STRUCTURE UPLOADED

=> d l11
L11 HAS NO ANSWERS
L11 STR



G1 O,S
G2 Ak,H

Structure attributes must be viewed using STN Express query preparation.

=> s l11
SAMPLE SEARCH INITIATED 14:37:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 80 TO ITERATE

100.0% PROCESSED 80 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1064 TO 2136
PROJECTED ANSWERS: 0 TO 0

L12 0 SEA SSS SAM L11

=> s l12 sss full
FULL SEARCH INITIATED 14:37:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1862 TO ITERATE

100.0% PROCESSED 1862 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

L13 10 SEA SSS FUL L11

=> s l2 sss full
FULL SEARCH INITIATED 14:38:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5455 TO ITERATE

100.0% PROCESSED 5455 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.02

L14 0 SEA SSS FUL L1

=> s l6 sss full
FULL SEARCH INITIATED 14:38:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 4599 TO ITERATE

100.0% PROCESSED 4599 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

```
L15             0 SEA SSS FUL L5

=> s l9 sss full
FULL SEARCH INITIATED 14:39:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    5472 TO ITERATE

100.0% PROCESSED    5472 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L16             0 SEA SSS FUL L8

=> s l11 sss full
FULL SEARCH INITIATED 14:40:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    1862 TO ITERATE

100.0% PROCESSED    1862 ITERATIONS                               10 ANSWERS
SEARCH TIME: 00.00.01

L17            10 SEA SSS FUL L11

=> FIL CAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                            1304.27    1304.48

FILE 'CAPLUS' ENTERED AT 14:41:01 ON 23 MAY 2005
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FILE COVERS 1907 - 23 May 2005  VOL 142 ISS 22
FILE LAST UPDATED: 22 May 2005  (20050522/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l13
L18             9 L13

=> d l18 ibib abs hitstr tot

L18  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:324179  CAPLUS
DOCUMENT NUMBER:          142:411656
TITLE:                    Synthesis of antibacterial biphenyl-containing
                          macrocycles for use in treating bacterial infections
                          in humans or animals
INVENTOR(S):              Lampe, Thomas; Adelt, Isabelle; Beyer, Dieter;
                          Brunner, Nina; Endermann, Rainer; Ehlert, Kerstin;
                          Kroll, Hein-Peter; Von Nussbaum, Franz; Raddatz,
```

Siegfried; Rudolph, Joachim; Schiffer, Guido; Schumacher, Andreas; Cancho-Grande, Yolanda; Michels, Martin; Weigand, Stefan

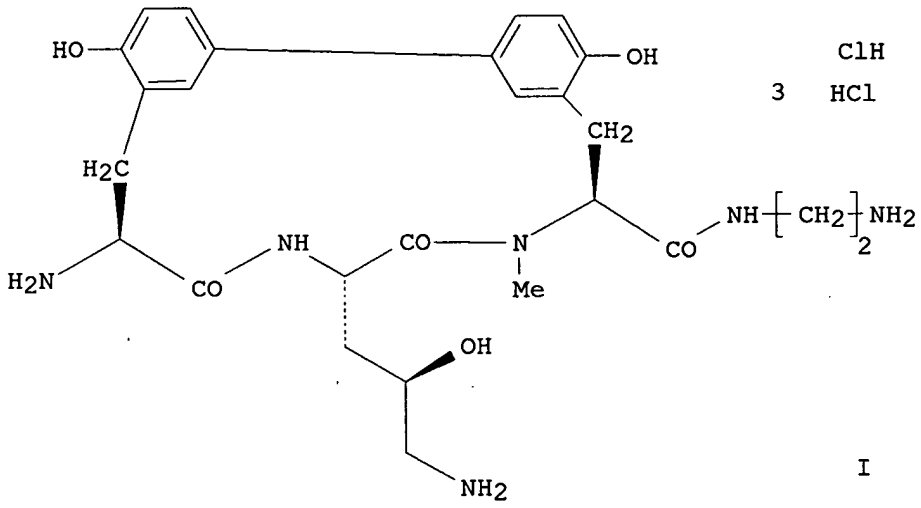
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033129	A1	20050414	WO 2004-EP10605	20040922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10358822	A1	20050421	DE 2003-10358822	20031216

PRIORITY APPLN. INFO.: DE 2003-10345724 A 20031001
DE 2003-10358822 A 20031216

GI



I

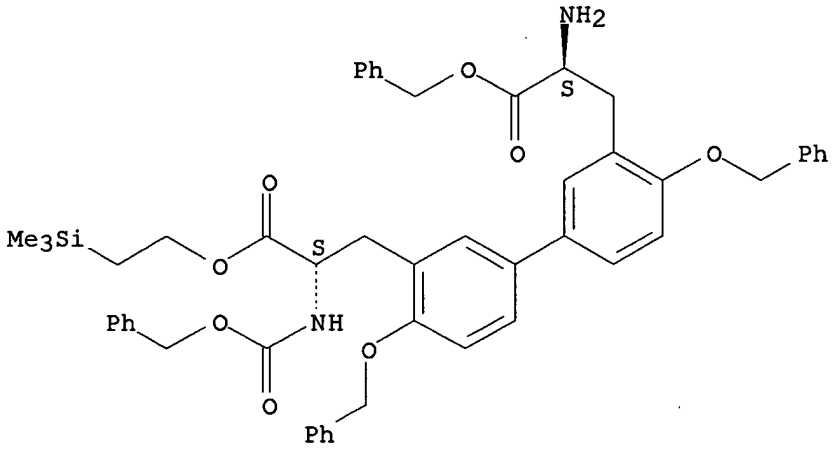
AB Macrocyclic biphenyl-containing oligopeptide amides, e.g., (I), analogs of biphenomycin B, were prepared for use in the treatment and prevention of bacterial infections in humans and animals. The biphenyl-linked dipeptide was first prepared, beginning from salicaldehyde, in 12 steps, followed by peptide coupling with an appropriate amino acid and macrocyclization. The resulting intermediate was coupled with a suitable amine-containing reactant to give title compds. as free bases or salts. In in vitro tests against S. aureus strains, including S. aureus 133, I was effective at min. blood concns. of 4 μg/mL. I had IC50 values in transcription-translation

tests against S. aureus 133 translation of 0.1 μM.

IT **636594-74-6P 849814-36-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antibacterial biphenyl-containing macrocyclic oligopeptides for
use in treatment of bacterial infections)

RN 636594-74-6 CAPLUS
CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-4,4'-bis(phenylmethoxy)-α'-[[(phenylmethoxy)carbonyl]amino]-, α-(phenylmethyl) α'-[2-(trimethylsilyl)ethyl] ester, monohydrochloride, (αS,α'S)- (9CI) (CA INDEX NAME)

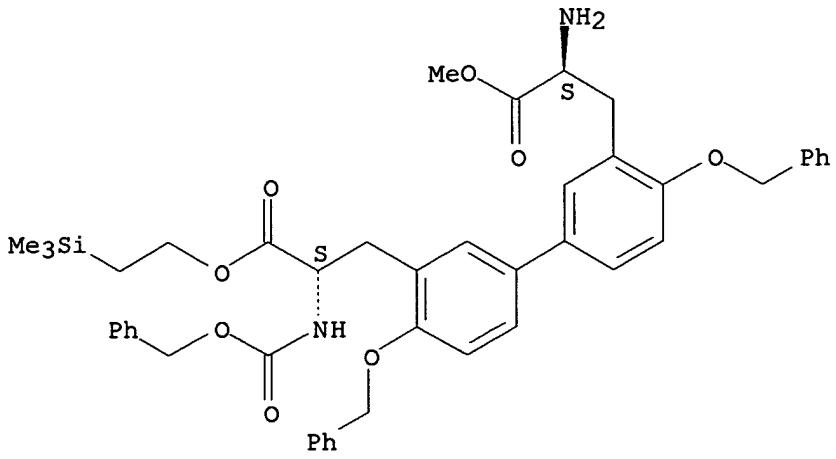
Absolute stereochemistry.



● HCl

RN 849814-36-4 CAPLUS
CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-4,4'-bis(phenylmethoxy)-α'-[[(phenylmethoxy)carbonyl]amino]-, α-methyl α'-[2-(trimethylsilyl)ethyl] ester, monohydrochloride, (αS,α'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

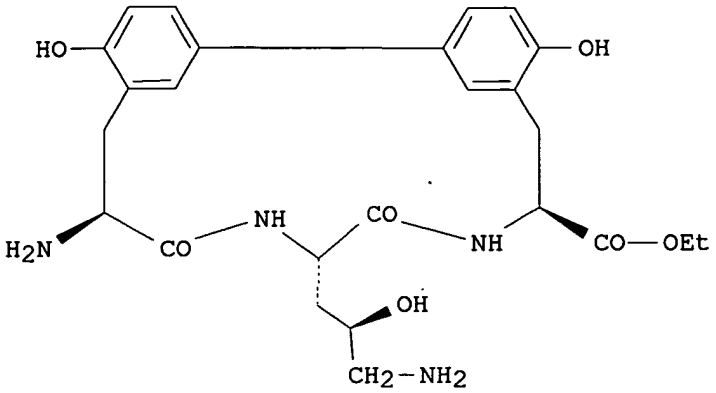
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:117114 CAPLUS
DOCUMENT NUMBER: 140:164239
TITLE: Antibacterial ester macro cycles
INVENTOR(S): Lampe, Thomas; Adelt, Isabelle; Beyer, Dieter; Brunner, Nina; Endermann, Rainer; Ehlert, Kerstin; Kroll, Hein-Peter; Von Nussbaum, Franz; Raddatz, Siegfried; Rudolph, Joachim; Schiffer, Guido; Schumacher, Andreas
PATENT ASSIGNEE(S): Bayer AG, Germany
SOURCE: Ger. Offen., 41 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10234422	A1	20040212	DE 2002-10234422	20020729
CA 2495479	AA	20040212	CA 2003-2495479	20030718
WO 2004012816	A1	20040212	WO 2003-EP7824	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1526896	A1	20050504	EP 2003-766214	20030718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: DE 2002-10234422 A 20020729
WO 2003-EP7824 W 20030718

OTHER SOURCE(S): MARPAT 140:164239
GI



I

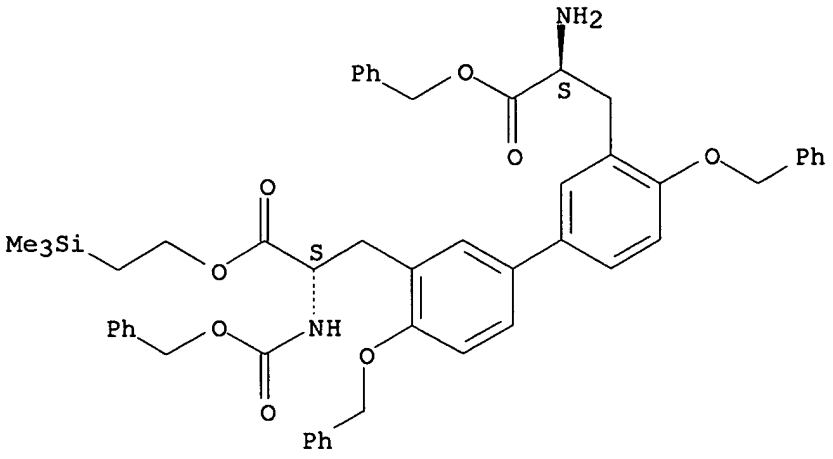
AB The present invention concerns compds., e.g. (I), procedures for their production, and pharmaceutical compns. containing them for use in the treatment of bacterial infections of humans or animals. The biphenyl system was constructed beginning with salicylaldehyde, which was 5-iodinated, O-benzylated, and reduced to the hydroxymethyl derivative, which was then brominated, replacing the hydroxy group. This intermediate was reacted with di-Et 2-tert-butoxycarbonylaminomalonate, followed by a mono-decarboxylation, to give (D/L)-N-Boc-2'-benzyloxy-5'-iodo-phenylalanine (II), which was then resolved to give pure (S)-II (ee >99%); this was C-protected as the benzyl ester, and part was reacted with bis(pinacolato)diborane to give intermediate (III). A second portion of II was transformed to the N-Cbz-protected form, and the acid esterified with 2-trimethylsilyl-ethanol to give intermediate (IV). Intermediates III and IV were reacted to give the chiral N,C-protected biphenyl portion of I (V). In a sep. sequence, t-Bu 5-Cbz-2(S)-Boc-amino-4(R)-hydroxypentanoate was used to prepare 4(R)-tBDMS-protected Boc-L-4-hydroxy-Nε-Cbz-ornithine, which was reacted with the Boc-deprotected V. Macrocyclization of the resulting intermediate consisted of activation of the second acid group as the pentafluorophenyl ester, and concurrent Boc-deprotection and cyclization to give the N',N", O,O'-protected I as its benzyl ester, which was deprotected/deesterified and re-esterified to give the Me or Et ester title compds. In in vitro tests against S. aureus 133 and B. catarrhalis M3, I was active at minimal blood concns. of 0.78 and 6.25 μM resp.; I had IC50 values in transcription-translation tests against E. coli and S. aureus 133 of 0.2 and 2.4-4.3 μM, resp.

IT **636594-74-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antibacterial biphenomycin B ester analogs for use in human or veterinary medicine)

RN 636594-74-6 CAPLUS

CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-4,4'-bis(phenylmethoxy)-α'-[[(phenylmethoxy)carbonyl]amino]-, α-(phenylmethyl) α'-[2-(trimethylsilyl)ethyl] ester, monohydrochloride, (αS,α'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



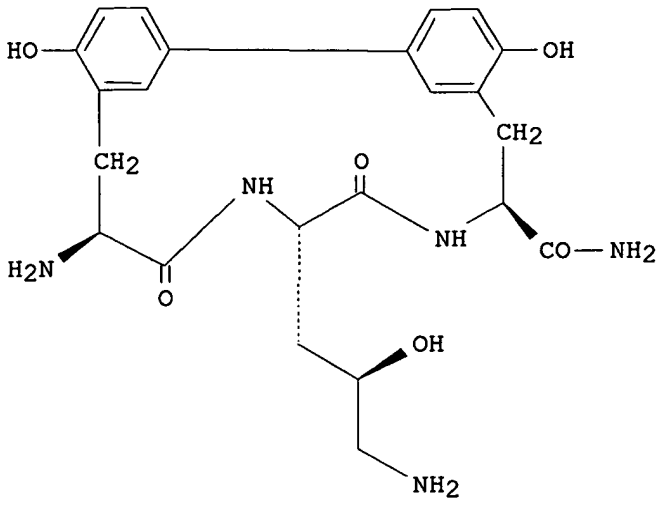
● HCl

L18 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1007003 CAPLUS
DOCUMENT NUMBER: 140:59934
TITLE: Synthesis of cyclic peptide macrolides for use in the treatment and prevention of bacterial infection
INVENTOR(S): Lampe, Thomas; Adelt, Isabelle; Beyer, Dieter; Brunner, Nina; Endermann, Rainer; Ehlert, Kerstin; Kroll, Hein-Peter; Von Nussbaum, Franz; Raddatz, Siegfried; Rudolph, Joachim; Schiffer, Guido; Schumacher, Andreas; Cancho-Grande, Yolanda; Michels, Martin; Weigand, Stefan
PATENT ASSIGNEE(S): Bayer Healthcare A.-G., Germany
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106480	A1	20031224	WO 2003-EP6078	20030610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10226921	A1	20031224	DE 2002-10226921	20020617
CA 2489454	AA	20041214	CA 2003-2489454	20030610
EP 1515983	A1	20050323	EP 2003-738012	20030610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011948	A	20050329	BR 2003-11948	20030610
PRIORITY APPLN. INFO.:			DE 2002-10226921 A	20020617

OTHER SOURCE(S): MARPAT 140:59934

GI



I

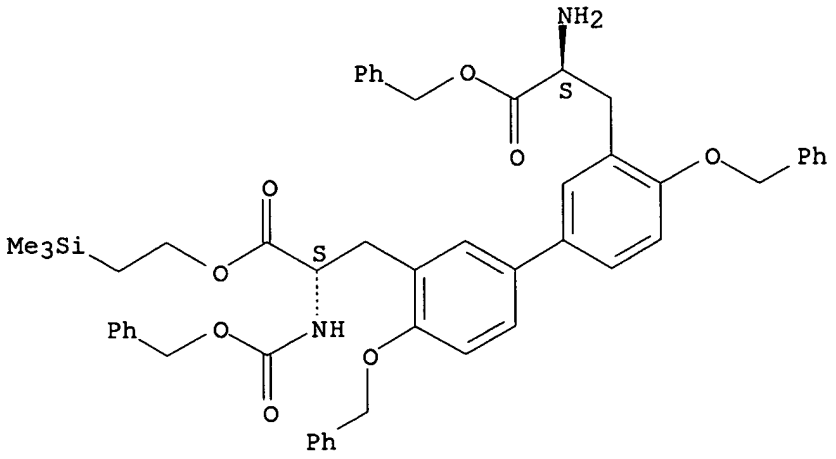
AB The invention relates to antibacterial amide macrocycles, e.g. (I), to methods for the production thereof, and to the use of the same for producing pharmaceuticals for the treatment and/or prophylaxis of illness, especially bacterial infections. Title compds. were synthesized beginning with salicylaldehyde, which was 5-iodinated, O-protected, reduced to the hydroxymethyl, brominated on the CH2 group, and coupled with di-Et 2-tert-butoxycarbonylaminomalonate, which, after decarboxylation and deesterification, gave the (DL)-N-Boc-protected 2'-benzyloxy-5'-iodo-phenylalanine (II). II was resolved into its pure D- and L-enantiomers; the L-II was protected as the N-Cbz derivative, then esterified with 2-(trimethylsilyl)ethanol, then reacted with (III) (prepared from II and 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi-1,3,2-dioxaborolane) to give biphenyl compound (IV). In a sep. reaction, (V) was prepared from the corresponding L-ornithine tert-Bu ester, the lactone opened and the alc. protected as the tert-butyldimethylsilyl derivative, and reacted with biphenyl IV, to give, after deprotection and amide formation, I as the dihydrochloride salt. In in vitro tests, using S. aureus, E. faecalis, B. catarrhalis, and E. coli strains, I had min. blood concentration effective ranges of 0.2-6.25 μM.

IT **636594-74-6P 636594-97-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biphenyl-containing cyclic peptide macrolides for use in the treatment and prevention of bacterial infection)

RN 636594-74-6 CAPLUS

CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-4,4'-bis(phenylmethoxy)-α'-[[(phenylmethoxy)carbonyl]amino]-, α-(phenylmethyl) α'-[2-(trimethylsilyl)ethyl] ester, monohydrochloride, (αS,α'S)- (9CI) (CA INDEX NAME)

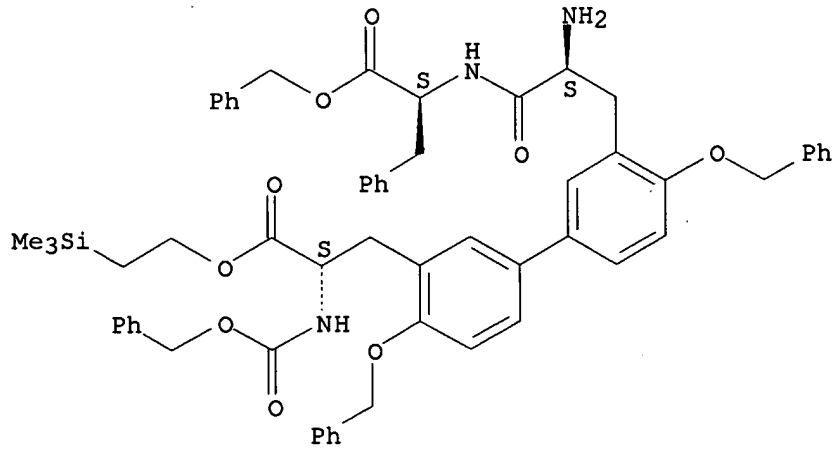
Absolute stereochemistry.



● HCl

RN 636594-97-3 CAPLUS
CN L-Phenylalanine, 3-[3'-[(2S)-3-oxo-2-[[(phenylmethoxy)carbonyl]amino]-3-[2-(trimethylsilyl)ethoxy]propyl]-4,4'-bis(phenylmethoxy)[1,1'-biphenyl]-3-yl]-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

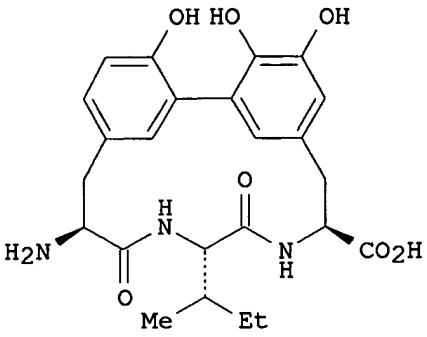
Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:345276 CAPLUS
DOCUMENT NUMBER: 139:180323
TITLE: Synthesis of the (S,S,S)-diastereomer of the 15-membered biaryl ring system of RP 66453
AUTHOR(S): Krenitsky, Paul J.; Boger, Dale L.
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, San Diego, CA, 92037, USA
SOURCE: Tetrahedron Letters (2003), 44(21), 4019-4022
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:180323
GI



I

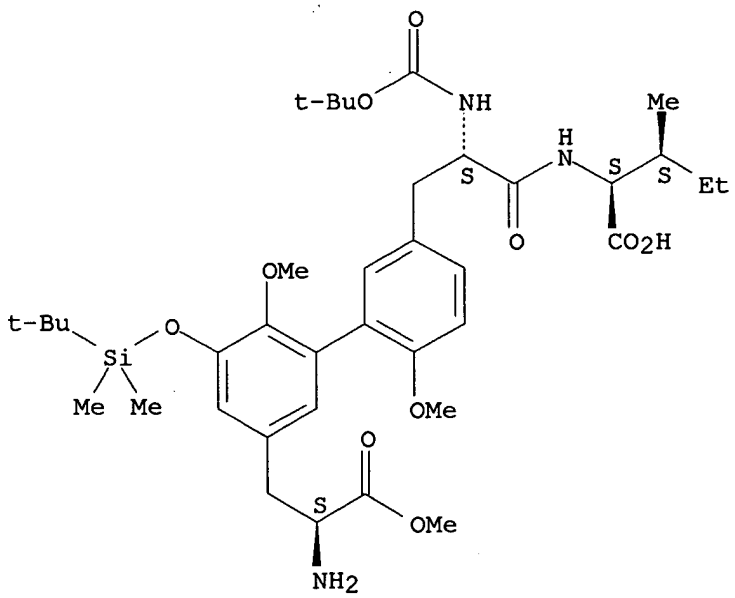
AB This work reports the synthesis of the 15-membered biaryl ring I, which constitutes an appropriately functionalized AB ring system of RP 66453.

IT **579469-86-6P 622338-03-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of the (S,S,S)-diastereomer of the 15-membered biaryl ring system of RP 66453)

RN 579469-86-6 CAPLUS

CN L-Isoleucine, 3-[5'-[(2S)-2-amino-3-methoxy-3-oxopropyl]-3'-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2',6-dimethoxy[1,1'-biphenyl]-3-yl]-N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl- (9CI) (CA INDEX NAME)

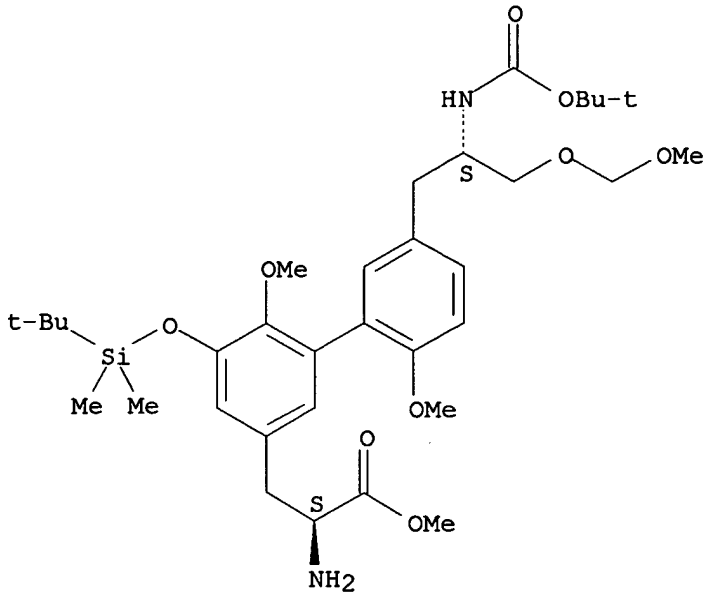
Absolute stereochemistry.



RN 622338-03-8 CAPLUS

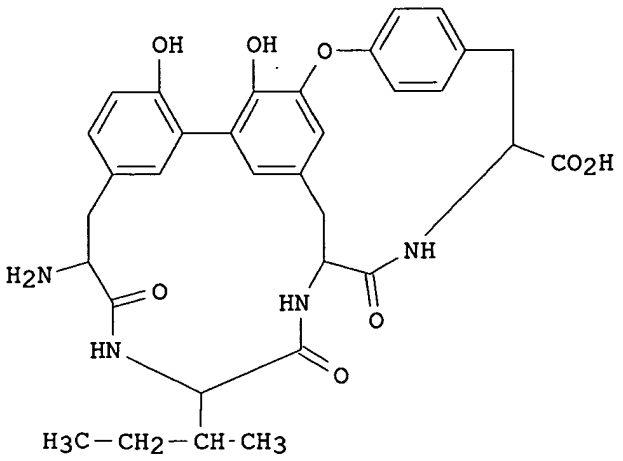
CN [1,1'-Biphenyl]-3-propanoic acid, α-amino-5'-[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-(methoxymethoxy)propyl]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2',6-dimethoxy-, methyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:211071 CAPLUS
DOCUMENT NUMBER: 137:93981
TITLE: Studies toward the total synthesis of RP-66453
AUTHOR(S): Boisnard, Sabine; Zhu, Jieping
CORPORATE SOURCE: CNRS, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, 91198, Fr.
SOURCE: Tetrahedron Letters (2002), 43(14), 2577-2580
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:93981
GI



I

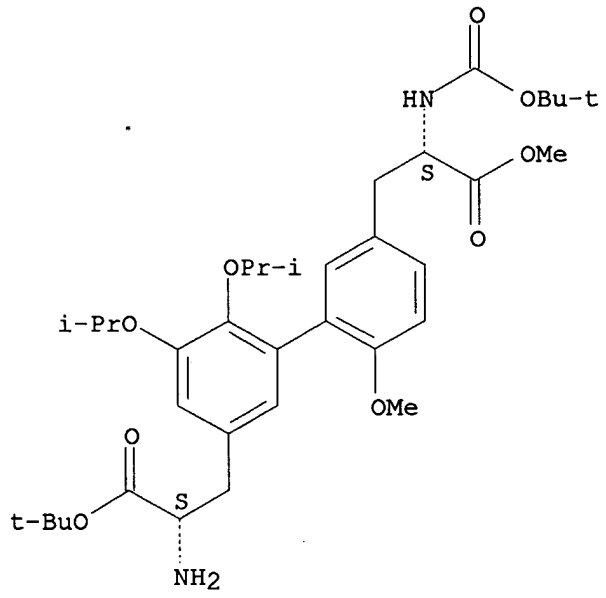
AB Synthesis of a bicyclic A-B-O-C ring system of RP-66453 (I), a neurotensine receptor antagonist, with an endo aryl-aryl and an endo aryl-aryl ether bond is described. An alternative synthetic strategy starting from the construction of functionalized B-O-C cycloisodityrosine unit is also detailed.

IT **351442-24-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the preparation of bicyclic A-B-O-C ring system of RP-66453)

RN 351442-24-5 CAPLUS

CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-α'-[[(1,1-dimethylethoxy)carbonyl]amino]-6'-methoxy-5,6-bis(1-methylethoxy)-, α-(1,1-dimethylethyl) α'-methyl ester, (αS,α'S)- (9CI) (CA INDEX NAME)

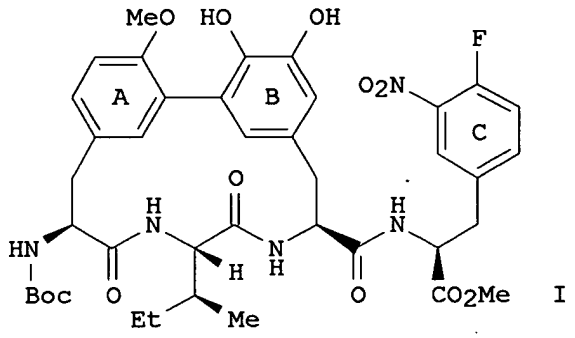
Absolute stereochemistry.



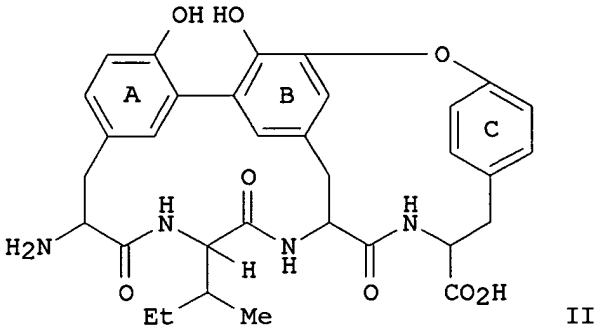
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:381070 CAPLUS
DOCUMENT NUMBER: 135:137701
TITLE: Studies on the Total Synthesis of RP 66453: Synthesis of Fully Functionalized 15-Membered Biaryl-Containing Macrocycle
AUTHOR(S): Boisnard, Sabine; Carbonnelle, Anny-Claude; Zhu, Jieping
CORPORATE SOURCE: Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, 91198, Fr.
SOURCE: Organic Letters (2001), 3(13), 2061-2064
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:137701
GI



I



II

AB Palladium-catalyzed Suzuki cross-coupling, Corey's enantioselective alkylation of glycine template, and macrolactamization are key steps in an efficient synthesis of the 15-membered macrocycle I, the A-B biaryl macrocyclic component of RP-66453 (II). Unfortunately, the cyclization of I by various methods (varying the base, the solvent and the temperature) did not provide the desired macrocycle II.

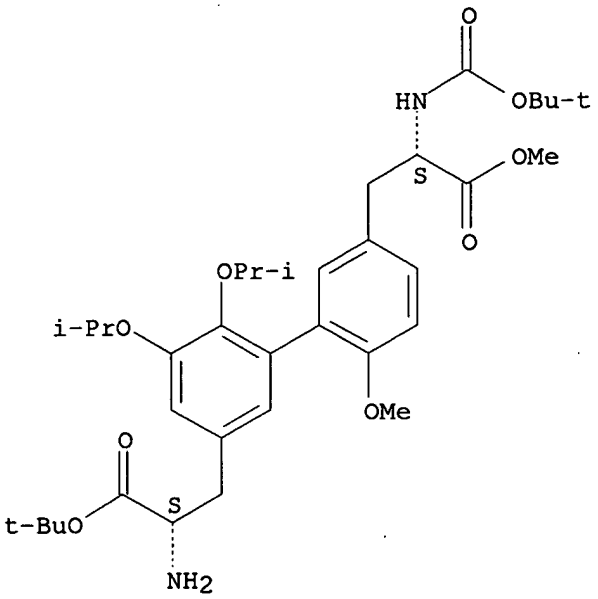
IT **351442-24-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of the fully functionalized biaryl, macrocyclic component of RP-66453)

RN 351442-24-5 CAPLUS

CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-α'-[[(1,1-dimethylethoxy)carbonyl]amino]-6'-methoxy-5,6-bis(1-methylethoxy)-, α-(1,1-dimethylethyl) α'-methyl ester, (αS,α'S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:445595 CAPLUS
DOCUMENT NUMBER: 125:137462
TITLE: N,N'-bisformyl dityrosine is an in vivo precursor of the yeast ascospore wall
AUTHOR(S): Briza, Peter; Kalchhauser, Hermann; Pittenauer, Ernst; Allmaier, Guenter; Breitenbach, Michael
CORPORATE SOURCE: Institut Genetik und Allemeine Biologie, Universitaet Salzburg, Salzburg, A-5020, Austria
SOURCE: European Journal of Biochemistry (1996), 239(1), 124-131
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

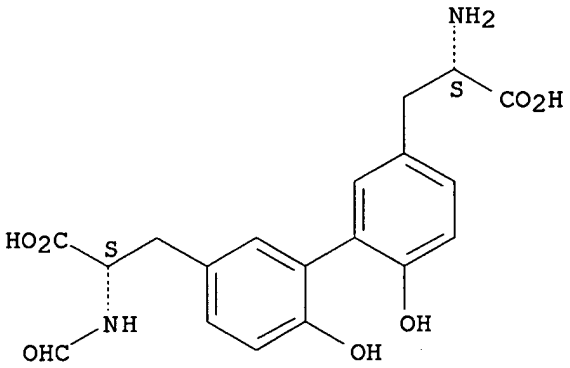
AB The amino acid, dityrosine, is a major component of he spore wall surface of the yeast Saccharomyces cerevisiae, where it is part of a highly cross-linked macromol. network of yet unknown chemical structure, consisting mostly of glucosamine, dityrosine and few other amino acids. Biosynthesis of the dityrosine moiety of this network consists of several steps, including the chemical modification of free L-tyrosine and the subsequent oxidative crosslinking of the modified tyrosine residues (catalyzed by a cytochrome P 450), leading to soluble dityrosine-containing spore wall precursors. We isolated, purified and characterized the dityrosine-containing precursor that appears late in spore wall synthesis and that is thought to be directly incorporated into the maturing spore wall. Chemical and spectroscopic analyses showed that this precursor is N,N'-bisformyl dityrosine. In addition, we identified a tyrosine-containing spore wall precursor as N-formyl tyrosine. The elucidation of the chemical structure of soluble spore wall precursors is crucial for the characterization of the function of the enzymes involved in maturation of the spore surface, e.g. by in vitro systems. A dityrosine-containing fragment, which was solubilized from mature spore walls by partial hydrolysis, was identified as N-formyl

dityrosine. Mature spore walls contain significant amts. of N-formyl dityrosine and N,N'-bisformyl dityrosine. This supports the assumption that the dityrosine-containing macromol. network on the spore surface has an unusual, nonpeptidic structure.

IT **179555-54-5P 179798-22-2P**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(N,N'-bisformyl dityrosine is in vivo precursor of yeast ascospore wall)

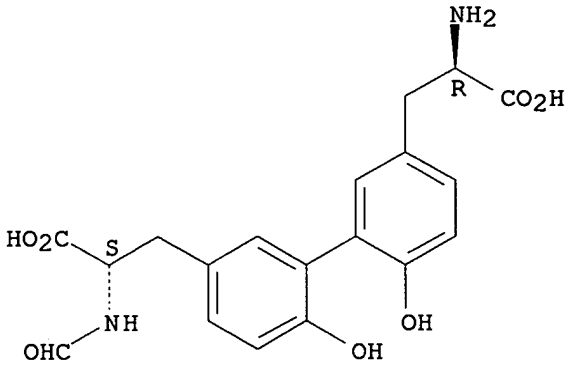
RN 179555-54-5 CAPLUS
CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-α'-(formylamino)-6,6'-dihydroxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 179798-22-2 CAPLUS
CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-α-(formylamino)-6,6'-dihydroxy-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L18 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:559729 CAPLUS
DOCUMENT NUMBER: 115:159729
TITLE: The synthesis of biphenomycin B [Erratum to document cited in CA114(25):247764b]
AUTHOR(S): Schmidt, Ulrich; Meyer, Regina; Leitenberger, Volker; Lieberknecht, Albrecht; Griesser, Helmut
CORPORATE SOURCE: Inst. Org. Chem. Isotopenforsch., Univ. Stuttgart, Stuttgart, 7000/80, Germany

SOURCE: Journal of the Chemical Society, Chemical Communications (1991), (10), 744
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English

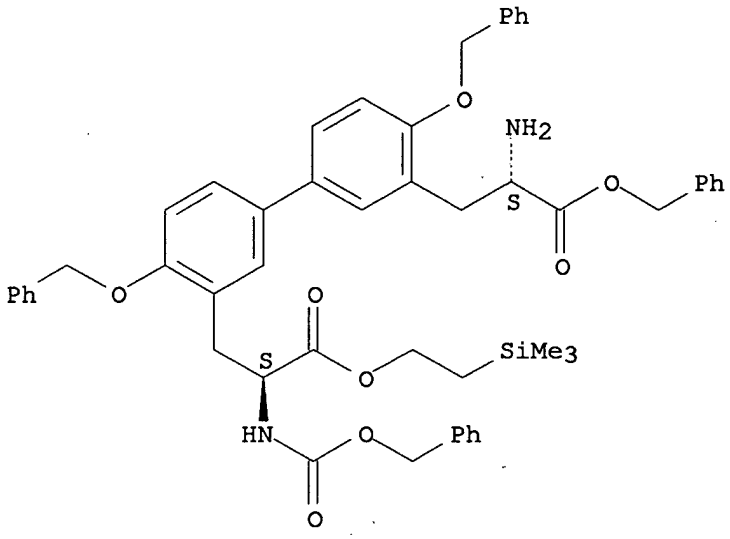
AB An error in the summary has been corrected Biphenomycin B is a highly potent antibiotic against Gram-pos. bacteria, not Gram-neg. as reported. The error was reflected in the abstract

IT **134038-83-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with hydroxyornithine derivative (Erratum))

RN 134038-83-8 CAPLUS

CN [1,1'-Biphenyl]-3,3'-dipropanoic acid, α-amino-4,4'-bis(phenylmethoxy)-α'-[[(phenylmethoxy)carbonyl]amino]-, α-(phenylmethyl) α'-[2-(trimethylsilyl)ethyl] ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:247764 CAPLUS
DOCUMENT NUMBER: 114:247764
TITLE: The synthesis of biphenomycin B
AUTHOR(S): Schmidt, Ulrich; Meyer, Regina; Leitenberger, Volker; Lieberknecht, Albrecht; Griesser, Helmut
CORPORATE SOURCE: Inst. Org. Chem. Isotopenforsch., Univ. Stuttgart, Stuttgart, 7000/80, Germany
SOURCE: Journal of the Chemical Society, Chemical Communications (1991), (5), 275-7
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:247764
GI